IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Hatcher et al.	)
		) Group Art Unit: 1618
Serial No.:	10/616,884	)
		)
Filed:	July 10, 2003	)
		) Examiner: Young, Micah Paul
For:	SOL-GEL DERIVED BIOACTIVE GLASS POLYMER COMPOSITE	)

APPEAL BRIEF

VIA EFS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I. REAL PARTY IN INTEREST

The real party in interest in this appeal is the University of Florida.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences know to Appellants, Appellants' legal representatives, or assignee that will directly affect, be directly affected by, or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

Claims 1 – 39 and 41 - 44 are pending in the application. Claim 40 has been canceled. Claims 1 - 10 are withdrawn. Claims 11 – 39 and 41 - 44 as they currently stand, are set forth in Appendix A on page 18 of this document. Appellants hereby appeal the final rejection of Claims 11 - 39 and 41 - 44.

IV. STATUS OF THE AMENDMENTS

No amendments have been filed in this particular application. In particular, no amendments have been filed subsequent to the Office Action dated September 29, 2009.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The incorporation of materials science, cellular biology and engineering together with other fields such as chemistry and biochemistry has contributed to the expansion of modern medicine. The integration of the physical and life sciences helps address a number of the key issues in fields such as biomaterials and tissue engineering with the goal of bringing functional and practical devices or implants to the patient. Engineered tissue scaffolds and implantable materials must maintain physical and mechanical properties necessary to withstand the dynamic conditions present within the body and be biocompatible.

A number of materials and a variety of scaffold designs have been investigated for use as tissue engineering matrices for bone regeneration applications. Ideally, the scaffold is a porous, three-dimensional structure capable of maintaining structural

integrity and allowing for cellular influx, growth, extracellular matrix (ECM) deposition, and metabolic exchange. The properties of the scaffold should be tailorable to control degradation rate, degree of porosity, and mechanical strength in order to closely match that of the host tissue. The scaffold material should not stimulate an adverse immunological response through chemical species present at the implant surface or through possible degradation byproducts (i.e., act as a biocompatible or bioactive material). To date, a number of synthetic polymers have been examined for their ability to serve as tissue engineering scaffolds. These materials have been examined in a number of forms such as particles, foamed porous scaffolds, and fibers, for their ability to initiate bone formation both in-vitro and in-vivo.

The use of bioactive glass fibers as tissue engineering scaffolds for the regeneration of new bone offers a number of advantages over the other forms mentioned above. The chemistry of this system is such that an immunological response is avoided and instead replaced with a bioactive mechanism. The bioactive glass fibers can undergo a series of chemical reactions leading to the precipitation of a hydroxyapatite (HA) layer on their surface, resulting in a chemical bond to the host tissue (Hench, LL and Wilson, J., "An Introduction to Bioceramics", World Scientific, 1993). The bioactive glass in turn becomes an integral part of the native tissue. Fabrication of a bioactive glass scaffolds constructed of fibers can provide the necessary structural integrity to maintain mechanical stability while at the same time allowing for the control of porosity, surface area, degradation rate, and the contact guidance of cells. The fibrous system mimics that of the natural collagen fibers orthogonally distributed within native bone providing it with enhanced strength. It is on these collagen fibrils that HA is deposited. In addition, the synthetic nature of the system allows for ease in production, transport and sterilization, making it an attractive option as a tissue engineering scaffold. Bioactive glass fibers have a relatively high silica content that limits their production by the classical high temperature commercial process due to extremely high melt viscosities.

Na_2O and CaO are usually necessary co-reactants in conventional processing to adjust the viscosity to levels compatible with fiber pulling. However, the high concentration of $Na_2O$and CaO in bioactive glasses induces crystallization, which ultimately limits the biological activity. Therefore, tradeoffs are generally required.

One way to overcome this problem is through the use of a sol-gel process, as opposed to a melt process, to produce fibers. The sol-gel process uses lower processing temperatures, which can reduce crystallization. A sol-gel process involves reactions of hydrolysis and condensation in metal alkoxides that lead to the formation of inorganic chains, rings, and clusters. These reactions can be controlled to produce the required sol structure (colloidal suspension) necessary to fabricate materials such as fibers, films, powders, and gels. Initial conditions of hydrolysis and condensation, such as, pH and concentration of agents can be used to adjust the resulting sol structure.

With regard to fiber pulling, the rheological behavior of the sol is one of the most important processing variables. It is basically accepted that elongated polymers in a solution is the main requirement for spinnability. Acidic pH values and low molar ratios between water and alkoxide are known to produce linear polymers that exhibit spinnability. On the other hand, high molar ratios between water and alkoxide and a basic medium led to production of spherical and ramified polymers that yield network formation. A low molar ratio of water:alkoxide (2: 1) favors generation of a functionality of 2 in the inorganic polymers. The functionality of 2, in this case, refers to the conversion of alkoxide groups to hydroxyl groups, which are more readily condensed and will produce a "linear" polymeric precursor of the sintered fiber. A higher functionality will lead to particle formation, which is undesirable for fiber production. An acidic medium reduces the immiscibility gap in the alcohol-alkoxide-water system and provides a catalytic effect that is also important in the development of linear polymers. Another important parameter of sol-gel fiber processing that should be optimized is the time between the onset of the spinnability and the gelation time. Disclosed formulations generally exhibit very short gelation times which restrict the production of continuous fibers and the process efficiency.

Support for the appealed claims is shown below.

11. A bioactive glass composite, comprising;

a biocompatible polymer, **(see paragraph [0015] on page 4)**

a bioactive glass including at least one calcium, and at least one phosphorous molecular species; **(see paragraph [0025] on page 6)** the biocompatible polymer being reacted with the bioactive glass, **(see paragraph [0062] on page 14)** wherein said

calcium and said phosphorous molecular species are not crystalline. (**See Figure 7; see also paragraphs [0060] through [0067]**)

12. The composite of claim 11, wherein said composite is in the form of microfibers, said fibers having a diameter less than 100 μm. **(see paragraph [0020] on page 5)**

13. The composite of claim 11, wherein said composite is in the form of particles, microspheres, or coatings. **(see paragraph [0018] on page 5)**

14. The composite of claim 12, wherein cells when seeded proliferate on said fibers. **(see paragraph [0019] on page 5)**

15. The composite of claim 14, wherein said cells are stem cells. **(see paragraph [0019] on page 5)**

16. The composite of claim 15, wherein said stem cells proliferate in the absence of any growth hormones. **(see paragraph [0019] on page 5)**

17. The composite of claim 12, wherein said fibers are substantially equally spaced to form an organized scaffold. **(see paragraph [0020] on page 5)**

18. The composite of claim 17, wherein said equal spacing is less than 50 μm. **(see paragraph [0020] on page 5)**

19. The composite of claim 17, wherein said equal spacing is less than 25 μm. **(see paragraph [0020] on page 5)**

20. (Previously presented) The composite of claim 11, wherein a porosity of said composition is at least 50%.**(see paragraph [0018] on page 5)**

21. The composite of claim 11, further comprising at least one biologically active agent. **(see paragraph [0021] on page 5)**

22. The composite of claim 21, wherein said composition forms an encapsulation layer around said biological agent. **(see paragraph [0021] on page 5)**

23. The composite of claim 21, wherein said biologically active agent is adsorbed onto the surface of said composition or chemically attached to a surface of said composition. **(see paragraph [0021] on page 6)**

24. The composite of claim 22, wherein said encapsulated biologically active agent is in the form of at least one selected from the group consisting of microcapsules, microspheres, microparticles, microfibers, sol gel matrices, and reinforcing fibers. **(see paragraph [0021] on page 5)**

25. The composite of claim 22, wherein said encapsulation layer is continuous, wherein a sustained release profile of said biologically active agent is provided. **(see paragraph [0021] on page 6)**

26. The composite of claim 11, further comprising at least one protein. **(see paragraph [0022] on page 6)**

27. The composite of claim 26, wherein said protein comprises at least one selected from the group consisting of collagen (including cross-linked collagen), fibronectin, laminin, elastin (including cross-linked elastin), osteonectin, bone sialoproteins (Bsp), alpha-2HS-glycoproteins, bone Gla-protein *(*Bgp*),* matrix Gla-protein, bone phosphoglycoprotein, bone phosphoprotein, bone proteoglycan, protolipids, bone morphogenetic protein, cartilage induction factor, platelet derived growth factor and skeletal growth factor. **(see paragraph [0022] on page 6)**

28. The composite of claim 11, wherein said composition is disposed on a surface of or

integrated within a medical device adapted for implantation into a patient. **(see paragraph [0023] on page 6)**

29. The composite of claim 28, wherein said medical device is a prosthetic device. **(see paragraph [0023] on page 6)**

30. A method of repairing hard or soft tissue defects, comprising the steps of:
applying a fiber composition comprising a biocompatible polymer, a bioactive glass including at least one calcium and at least one phosphorous molecular species to a defect site on a patient, **(see paragraph [0020] on page 5)**

wherein said calcium and said phosphorous molecular species are not crystalline. **(See Figure 7; see also paragraphs [0060] through [0067])**

31. The method of claim 30, wherein said composition is in the form of microfibers, said fibers having a diameter less than 100 μm. **(see paragraph [0018] on page 5)**

32. The method of claim 30, wherein said fibers are substantially equally spaced to form an organized scaffold. **(see paragraph [0020] on page 5)**

33. The method of claim 30, wherein said equal spacing is less than 50 μm. **(see paragraph [0020] on page 5)**

34. The method of claim 30, where said composition is in the form of particles. **(see paragraph [0018] on page 5)**

35. The method of claim 30, wherein cells proliferate on or around said composition in the absence of any growth hormones. **(see paragraph [0019] on page 5)**

36. A method of forming a bioactive glass, comprising the steps of:

mixing a biocompatible polymer, a gelable inorganic base material, and

at least one calcium and phosphorous molecular species, **(see paragraph [0025] on page 6)** and

hydrolizing said mixture, **(see paragraph [0025] on page 6)** wherein said calcium and said phosphorous molecular species are not crystalline. **(See Figure 7; see also paragraphs [0060] through [0067])**

37. The method of claim 36, further comprising the step of forming a plurality of fibers, wherein said forming process is at a temperature of no more than 200 C. **(see paragraph [0025] on page 6)**

38. The method of claim 37, wherein said forming step comprises air-spraying or extruding. **(see paragraph [0065] on page 15)**

39. The composite of claim 11, wherein said glass is a continuous phase inorganic network. **(see paragraph [0015] on page 4)**

41. The composite of claim 11, wherein said bioactive glass comprises a gelled inorganic material containing at least one calcium and at least one phosphorous molecular species. **(see paragraph [0018] on page 5)**

42. The composite of claim 41, wherein said gelled inorganic material comprises at least one gelled alkoxysilane. **(see paragraph [0015] on page 4)**

43. The composite of claim 41, wherein said gelled inorganic material comprises at least one gelled non-alkoxysilane alkoxide selected from the group consisting of alurninates, titanates, and borates. **(see paragraph [0015] on page 4)**

44. The composite of claim 11, wherein said biocompatible polymer comprises at least one selected from the group consisting of polyvinylpyrrolidone (PVP), polyethyleneimine (PEI), polycarboxylmethylcellulose (PCMC), polyethylenglycol (PEG), polypropylene oxide (PPO), polyvinylalcohol (PVA), polyacrylic acid (PAA), polymethylacrylic acid

(PMAA), polystyrene sulfonic acid (PSSA), and gelatin. **(see paragraph [0015] on page 4)**

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Claims 11, 13, 21- 25, 28, 30, 34, 36, 37, 39, 41 42 and 44 are rejected under 35 U.S.C. §102 (a) as being anticipated by U.S. Patent No. 6,328,990 to Ducheyne et al. (hereinafter "Ducheyne"). (Office Action dated 09-25-2009, page 2)

2. Claims 11 – 17, 28 – 32, 34, 35, 38 and 41 – 42 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,721,049 to Marcolongo et al. (hereinafter "Marcolongo") (Office Action dated 09-25-2009, page 3)

3. Claims 11, 13, 21 – 29, 34 – 39, 41, 42 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of U.S. Patent No. 6,328,990 to Ducheyne in view of U.S. Patent No. 5,591,453 to Ducheyne (hereinafter Ducheyne '453). (See Office Action dated 09-25-2009, page 5)

4. Claims 11, 12, 14, 18 – 20, 30 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Ducheyne in view of U. S. Patent No. 5,711,960 to Shikinami (hereinafter Shikinami). (Office Action 09-25-2009, page 7)

VII. ARGUMENT

1. Claims 11, 13, 21- 25, 28, 30, 34, 36, 37, 39, 41 42 and 44 are patentable over Ducheyne.

In making the rejection, the Examiner has stated that the claims are drawn to a bioactive glass composite comprising biocompatible polymer and a bioactive glass. (Office Action dated 10-03-08, page 2)

To anticipate a claim under 35 U.S.C. § 102, a single source must contain all of the elements of the claim. *Lewmar Marine Inc. v. Barient, Inc.*, 827 F.2d 744, 747, 3 U.S.P.Q.2d 1766, 1768 (Fed. Cir. 1987), *cert. denied*, 484 U.S. 1007 (1988).

Claim 11 is directed to a bioactive glass composite, comprising a biocompatible polymer, a bioactive glass including at least one calcium, and at least one phosphorous molecular species; the biocompatible polymer being reacted with the bioactive glass, wherein said calcium and said phosphorous molecular species are not crystalline.

Ducheyne is directed to a 'bioactive, degradable composite material and to composite material microspheres." (See Abstract) Ducheyne teaches

> Glass powders with a size <20 μm and a composition of 45% SiO_2, 24.5% CaO, 24.5% Na_2O, and 6% P_2O_5 (in % by weight) were used. The glass powders were modified by immersion in a 0.05 M Tris buffer (pH 7.3) supplemented with plasma electrolyte (a simulated physiological solution; ion concentrations as in Radin, S.R. and P. Ducheyne 1993. J. Biomed. Mater. Res. 27:35-45) at 37° C. The immersed particles were shaken and incubated from 1 hour to 3 days.

(See Col. 2, lines 55 – 61)

Ducheyne teaches pre-immersing the glass powders for three days in order to complete modification and that this modification prevents cracking of the composites. (See Col. 3, lines 14 – 18) Ducheyne teaches that the glass powders must be immersed for three days before the modification process to be complete:

> After immersion in simulated physiological solution for 6 hours, amorphous calcium phosphate was formed as indicated by the presence of a bending vibration mode of the PO_4 groups (P-O bend). After immersion for 1 day, the P-O bend peak divided, indicating the presence of crystalline calcium phosphate ceramic phase. The appearance of bands located at 870 cm^{-1} (C-O bonds) and 960 cm^{-1} (P-O symmetric stretch, characteristic of hydroxyapatite) indicated that the crystalline phase could be identified as carbonated calcium hydroxyapatite.

(See Col. 3, lines 1 – 9)

Ducheyne further teaches that:

> For instance, bioactive glass particles immersed for 3 days were used in preparation of microspheres of the composite material of the present invention.

(See Col. 3, lines 1 – 9) Since Ducheyne teaches that after immersion for one day, the glass spheres are crystalline and that modified glass spheres muse be immersed for 3 days before being blended with polylactic acid (PLA) microspheres, it is submitted that Ducheyne teaches blending crystalline glass powders with a polymer. The claimed

invention in contrast is directed to a biocompatible polymer that is reacted with the bioactive glass, wherein said calcium and said phosphorous molecular species are not crystalline. For this reason at least, Ducheyne does not teach all elements of the claimed invention.

Ducheyne also does not teach that the glass powder is reacted with the polymer. Ducheyne is silent as to a reaction between the glass powder and the polymer. The glass powder and the polylactic acid disclosed by Ducheyne do not have any reactive species on them. For this reason too, Ducheyne does not teach all elements of the claimed invention.

Ducheyne therefore does cannot anticipate the claimed invention. The Applicants respectfully request a withdrawal of the anticipation rejection and an allowance of the claims.

2. Claims 11 – 17, 28 – 32, 34, 35, 38 and 41 – 42 are patentable over Marcolongo.

In making the rejection, the Examiner has stated that "[T]he glass can is extruded at high temperature resulting in an amorphous glass material (Col.5, lines 35 – 50) (Office Action dated 09-25-2009, page 3) This is patently inaccurate.

In making the rejection, the Examiner states that "Regarding the claim limitation drawn to the biocompatible polymer **reacting** with the bioactive glass compound, it is the position of the Examiner that such a limitation does not differentiate the claims over the prior art. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe*, 777 F.2d 695,698,227 USPQ 964,966 (Fed. Cir. 1985). In the instant case the instant claims are defined by a composite comprising a biocompatible polymer and a bioactive glass." This too is completely inaccurate.

Marcolongo teaches "[C]omposite materials formed from bone bioactive glass or ceramic fibers and structural fibers." (See Abstract) Marcolongo teaches that the

preferred composition leads to a slowly reacting glass. (See Col. 4, lines 43 – 45)

Marcolongo teaches that:

> A slow reaction rate is desired because a large surface area of glass is exposed to physiological solutions during implantation with glass in a fibrous configuration. A bioactive glass that quickly degrades may lead to an adverse inflammatory response, impeding bone growth and bonding. The tradeoff is that since the glass must be drawn into continuous fibers it cannot be too viscous or too fluid, or the fibers would break upon drawing.

(See Col. 4, lines 45 – 50) Marcolongo teaches that the glass is slow reacting so that it may become compatible with body tissue. Marcolongo does not teach that the glass reacts with the polymer as presently claimed.

With regard to the Examiner's contention that the term "reacting" represents a product by process limitation, the Applicants respectfully disagree. In the first instance, the Applicants have not used the term "reacting" but have used the term "reacted." The term "reacted" represents a structural limitation and indicates that the biopolymer is bonded with the bioactive glass. The Applicants have used this limitation because this is the best manner to claim the product. The Examiner's statement that "in the instant case the instant claims are defined by a composite comprising a biocompatible polymer and a bioactive glass" is blatantly inaccurate. The claims must be construed as involving a biocompatible polymer that is reacted with a bioactive glass. The courts have consistently held that a term that "can connote with equal force a structural characteristic of the product or a process of manufacture are commonly and **by default interpreted in their structural sense**, unless the patentee has demonstrated otherwise." *3M Innovative Props. Co. v. Avery Dennison Corp.*, 350 F.3d 1365, 1371-72 (Fed. Cir. 2003). For example, the CCPA held that

> [T]he recitation of the particles as 'interbonded one to another by interfusion between the surfaces of the perlite particles' is as capable of being construed as **a structural limitation** as 'intermixed,' 'ground in place,' 'press fitted,' 'etched,' and 'welded,' all of which at one time or another have been separately held capable of construction as structural, rather than process, limitations.

In re Garnero, 412 F.2d 276, 279 (C.C.P.A. 1969); *see also AFG Indus., Inc. v. Cardinal*

IG Co., Inc., 375 F.3d 1367, 1372-73 (Fed. Cir. 2004) (holding that the term 'multiple depositions' does not refer to a process but is only relevant if multiple depositions "affect the **structure** and optical properties" of the claimed material"); *Vanguard Prods. Co. v. Parker Hannifin Corp.*, 234 F.3d 1370, 1372 (Fed. Cir. 2000) (holding that the claim term "integral" describes a **structural relation**, not the particular manufacturing process related in the specification); *Hazani v. United States Int'l Trade Comm'n*, 126 F.3d 1473, 1479 (Fed. Cir. 1997) ("the 'chemically engraved' limitation, read in context, describes the product more by its **structure** than by the process used to obtain it.").

Marcolongo teaches that

> A most preferred composition that can be successfully drawn into fibers while maintaining bioactivity is: 52% SiO_2; 30% Na_2O; 15% CaO; 3% P_2O_5. In developing this range, experimental trials showed that a composition of 52% SiO_2; 32% CaO; 3% P_2O_5; 13% Na_2O; would be bioactive, however, it is difficult to draw this composition of glass into fibers.

(See Col. 4, lines 55 – 62) Marcolongo in its examples, teaches that polysulfone is used as a polymer. Marcolongo does not teach or suggest that either the polysulfone or the metal oxides (SiO_2; Na_2O; CaO; P_2O_5) listed above are capable of reacting with each other. Neither the polysulfone nor the metal oxides of Marcolongo have any reactive species that are capable of reacting with one another.

Marcolongo, in not teaching reacting, does not teach all elements of the claimed invention.

In addition, the Examiner has alleged that "[T]he glass can is extruded at high temperature resulting in an amorphous glass material (Col.5, lines 35 – 50)". A review of lines 35 – 50 in Column 5 of Marcolongo does not reveal the use of the word "amorphous". Marcolongo thus does not teach that the untreated glass is amorphous when it is blended with the polysulfone in lines 35 – 50 of Column 5. For this reason too, it is submitted that Marcolongo does not teach all elements of the claimed invention. Since Marcolongo does not teach that the glass is reacted with the polymer, it does not teach all elements of the claimed invention. The Applicants respectfully request a withdrawal of the anticipation rejection and an allowance of the claimed invention.

3. Claims 11, 13, 21 – 29, 34 – 39, 41, 42 and 44 are patentable over Ducheyne in view of Ducheyne '453.

The Supreme Court has recently reaffirmed the principle that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the art.... This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *KSR Int'l. Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007). The Court further stated that "[r]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *Id.* (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)). However, "the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* And the Court expressly encouraged the use of common sense in such analysis. *Id.* Finally, the Court agreed that the teaching-suggestion-motivation test ("TSM test") captured a helpful insight to prevent hindsight bias, but the Court held that "[h]elpful insights, however, need not become rigid and mandatory formulas; and when it is so applied, the TSM test is incompatible with our precedents." *Id.*

The arguments incorporated above against Ducheyne are incorporated herein by reference. In particular, Ducheyne does not teach that the glass is not crystalline. It also does not teach that the polymer is reacted with the glass.

Ducheyne '453 is directed to manufacturing carriers for biologically active molecules from a sol-gel derived process. (see Abstract; see also see also Col. 8, lines 42 – 47) Ducheyne '453 teaches that the sol-gel derived process involves a reaction between a metal alkoxide, such as tetramethylorthosilicate and calcium methoxyethoxide. (See Col. 13, lines 18 – 40) Phosphorus is derived from triethyl phosphate. (See Col. 13, line 41)

Ducheyne '453 does not teach that the reaction between the metal alkoxide, the tetramethylorthosilicate and the calcium methoxyethoxide involves a reaction with a polymer. Ducheyne '453 thus does not teach that the bioactive glass is reacted with a

bioactive polymer. Ducheyne '453 thus does not make up for the deficiency of Ducheyne.

Ducheyne '453 also does not teach or suggest that the reaction product obtained from the reaction between the metal alkoxides and the phosphate results in an amorphous product. Ducheyne '453 once again does not make up for the deficiency of Ducheyne. Since Ducheyne '453 even when combined with Ducheyne does not teach all elements of the claimed invention, the Applicants believe that the Examiner has not made a prima facie case of obviousness over Ducheyne '453 in view of Ducheyne. The Applicants respectfully request a withdrawal of the obviousness rejection and an allowance of the claims.

4. Claims 11, 12, 14, 18 – 20, 30 and 33 are patentable over the combined disclosures of Ducheyne in view of Shikinami.

The claims are drawn to a biocompatible composite comprising a biocompatible polymer, bioactive glass in the form of fibers that act as a scaffold. (See Office Action dated 09-25-2009, page 7)

The arguments incorporated above against Ducheyne are incorporated herein by reference. In particular, Ducheyne does not teach that the glass is not crystalline. It also does not teach that the polymer is reacted with the glass.

Shikinami teaches an implant material which has high mechanical strength and durability in three-dimensional directions. (see Abstract) Shikinami teaches that the implant material functions to synchronize with the deformation characteristics of surrounding biological tissues and is capable of being penetrated by biological tissues into its fabric space. (see Abstract)

Shikinami teaches that the implant material uses as a base material, a biocompatible bulk structure of a three-dimensionally woven or knitted fabric of organic fibers or a composite fabric thereof, and its void ratio in the fabric is preferably set to 20 to 90 vol%. (see Abstract) The base material comprises a biocompatible bulk structure of a tri-axial or more three-dimensionally woven fabric of organic fibers, a tri-axial or more three-dimensionally knitted fabric of organic fibers or a combination thereof. (see Claim 1)

Shikinami in its Examples teaches the manufacturing of this three-dimensional woven fabric. Shikinami in Col. 7, line 25 through Col. 8, line 27 teaches how to manufacture a glass coated yarn. Only relevant portions of the disclosure of Shikinami are disclosed below to point out the differences between Shikinami and the claimed invention.

In its Example 1, Shikinami teaches that a high density polyethylene (HDPE) yarn of 50 denier filaments is coated with linear low-density polyethylene (LLDPE) (melted at 120°C), which is then subjected to a plasma treatment. (See Col. 17, lines 25 – 67) Following the plasma treatment, the yarn of Shikanami is subjected to treatment in a phosphate solution and a calcium containing solution to produce a thin layer of calcium phosphate on the yarn. (See Col. 18, lines 1 – 7) The yarn is then used to produce a three-dimensional weave of a block shaped orthogonal fabric. (See Col. 18, lines 8 – 20) The weave is then placed in a mold and pressurized following, which it is coated with a fine particle powder of AW glass. (See Col. 18, lines 21 – 27)

Shikinami thus teaches manufacturing a weave from a yarn having a layer of calcium phosphate disposed on it with a layer of glass particles disposed upon the surface of the weave. Shikanami does not state that its calcium and phorphorus species are not crystalline as presently claimed. Shikanami thus does not rectify the deficiency of Ducheyne.

Thus, Ducheyne, even when combined with Shikinami would not produce the claimed invention. Since neither Ducheyne nor Shikinami teach all elements of the claimed invention, there is no motivation to combine Ducheyne with Shikinami.

In addition, neither Ducheyne nor Shikanami teaches that the glass is reacted with the polymer. In making the rejection, the Examiner has stated that "[O]nce the Examiner provides rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to the Applicant to come forward with evidence produced by a different process, the burden shifts to the Applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product." (See Office Action dated 09-25-2009, page 8)

In the first instance the Examiner has produced no rationale for why the

Applicants claim is a product by process limitation and not a structural limitation. The Applicants contend that the term "reacted" is a structural limitation and not a product-by-process limitation. As noted above, the Applicants believe that the term "reacted" indicates that the polymer is reacted with the glass. The examples of the Applicants invention clearly explain to one of ordinary skill in the art that the precursors to the glass involve reactive metal alkoxides. Neither Ducheyne nor Shikanami use these metal alkoxides or any other species that undergo a reaction with the respective polymers. The Applicants believe that the Examiner's contention that the term "reacted" is a product-by-process limitation is misguided and stems from an inadequate knowledge of both chemistry and the law.

In summary, the Applicants believe that the Examiner has not made a prima facie case of obviousness over Ducheyne when combined with Shikinami. The Applicants therefore respectfully request a withdrawal of the obviousness rejection over Ducheyne in view of Shikinami.

VIII. CLAIMS APPENDIX

APPENDIX A

11. A bioactive glass composite, comprising;
a biocompatible polymer,
a bioactive glass including at least one calcium, and at least one phosphorous molecular species; the biocompatible polymer being reacted with the bioactive glass, wherein said calcium and said phosphorous molecular species are not crystalline.

12. The composite of claim 11, wherein said composite is in the form of microfibers, said fibers having a diameter less than 100 μm.

13. The composite of claim 11, wherein said composite is in the form of particles, microspheres, or coatings.

14. The composite of claim 12, wherein cells when seeded proliferate on said fibers.

15. The composite of claim 14, wherein said cells are stem cells.

16. The composite of claim 15, wherein said stem cells proliferate in the absence of any growth hormones.

17. The composite of claim 12, wherein said fibers are substantially equally spaced to form an organized scaffold.

18. The composite of claim 17, wherein said equal spacing is less than 50 μm.

19. The composite of claim 17, wherein said equal spacing is less than 25 μm.

20. The composite of claim 11, wherein a porosity of said composition is at least 50%.

21. The composite of claim 11, further comprising at least one biologically active agent.

22. The composite of claim 21, wherein said composition forms an encapsulation layer around said biological agent.

23. The composite of claim 21, wherein said biologically active agent is adsorbed onto the surface of said composition or chemically attached to a surface of said composition.

24. The composite of claim 22, wherein said encapsulated biologically active agent is in the form of at least one selected from the group consisting of microcapsules, microspheres, microparticles, microfibers, sol gel matrices, and reinforcing fibers.

25. The composite of claim 22, wherein said encapsulation layer is continuous, wherein a sustained release profile of said biologically active agent is provided.

26. The composite of claim 11, further comprising at least one protein.

27. The composite of claim 26, wherein said protein comprises at least one selected from the group consisting of collagen (including cross-linked collagen), fibronectin, laminin, elastin (including cross-linked elastin), osteonectin, bone sialoproteins (Bsp), alpha-2HS-glycoproteins, bone Gla-protein (Bgp), matrix Gla-protein, bone phosphoglycoprotein, bone phosphoprotein, bone proteoglycan, protolipids, bone morphogenetic protein, cartilage induction factor, platelet derived growth factor and skeletal growth factor.

28. The composite of claim 11, wherein said composition is disposed on a surface of or integrated within a medical device adapted for implantation into a patient.

29. The composite of claim 28, wherein said medical device is a prosthetic device.

30. A method of repairing hard or soft tissue defects, comprising the steps of:

applying a fiber composition comprising a biocompatible polymer, a bioactive glass including at least one calcium and at least one phosphorous molecular species to a defect site on a patient, wherein said calcium and said phosphorous molecular species are not crystalline.

31. The method of claim 30, wherein said composition is in the form of microfibers, said fibers having a diameter less than 100 μm.

32. The method of claim 30, wherein said fibers are substantially equally spaced to form an organized scaffold.

33. The method of claim 30, wherein said equal spacing is less than 50 μm.

34. The method of claim 30, where said composition is in the form of particles.

35. The method of claim 30, wherein cells proliferate on or around said composition in the absence of any growth hormones.

36. A method of forming a bioactive glass, comprising the steps of:

mixing a biocompatible polymer, a gelable inorganic base material, and at least one calcium and phosphorous molecular species, and

hydrolizing said mixture, wherein said calcium and said phosphorous molecular species are not crystalline.

37. The method of claim 36, further comprising the step of forming a plurality of fibers, wherein said forming process is at a temperature of no more than 200 C.

38. The method of claim 37, wherein said forming step comprises air-spraying or extruding.

39. The composite of claim 11, wherein said glass is a continuous phase inorganic network.

41. The composite of claim 11, wherein said bioactive glass comprises a gelled inorganic material containing at least one calcium and at least one phosphorous molecular species.

42. The composite of claim 41, wherein said gelled inorganic material comprises at least one gelled alkoxysilane.

43. The composite of claim 41, wherein said gelled inorganic material comprises at least one gelled non-alkoxysilane alkoxide selected from the group consisting of alurninates, titanates, and borates.

44. The composite of claim 11, wherein said biocompatible polymer comprises at least one selected from the group consisting of polyvinylpyrrolidone (PVP), polyethyleneimine (PEI), polycarboxylmethylcellulose (PCMC), polyethylenglycol (PEG), polypropylene oxide (PPO), polyvinylalcohol (PVA), polyacrylic acid (PAA), polymethylacrylic acid (PMAA), polystyrene sulfonic acid (PSSA), and gelatin.

IX. EVIDENCE APPENDIX

No evidence has been submitted in connection with this appeal brief.

X. RELATED PROCEEDINGS APPENDIX

There have been no related proceedings in connection with this appeal brief. As a result there are no decisions rendered by a court or the Board pursuant to paragraph (c)(1)(ii) of this section.

XI. CONCLUSION

It is believed that the foregoing amendments and remarks fully comply with the Office Action and that the claims herein should now be allowable to Applicants. Accordingly, reconsideration and allowance is requested.

If there are any additional charges with respect to this Amendment or otherwise, please charge them to Deposit Account No. 06-1130 maintained by Assignee.

Respectfully submitted,

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